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(21) International Application Number: PCT/IT97/00133 (22) International Filing Date: 12 June 1997 (12.06.97) (71)(72) Applicant and Inventor: SACCHETTI, Antonio [IT/IT]; Via Campodimele, 75, I-00189 Roma (IT). (74) Agent: SARPI, Maurizio; Studio Ferrario, Via Collina, 36, I-00187 Roma (IT).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: NATURAL BROAD-SPECTRUM ANTIBIOTIC		
(57) Abstract		
<p>There is disclosed a natural broad-spectrum antibiotic formed of a mixture of Tea Tree Oil (Essential Oil of <i>Malaleuca Alternifolia</i>) and Thyme Essential Oil in the ratio of 50-90 % and 50-10 % by weight, respectively.</p>		

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Natural broad-spectrum antibiotic

5 The present invention relates to a natural broad-spectrum antibiotic consisting of the combination of two essential oils of vegetal origin, the antibacterial activity of which is synergically enhanced. Said natural antibiotic is particularly active against both gram-positive and gram-negative bacteria as well as against Candida which is, as known, antibiotic-fast, some antibiotics even assisting the growth of the latter.

10 The investigations about even more active antibiotic molecules kept the bacterial synthesis away from what may be said natural so that recent molecules certainly are very effective but also have a high toxicity. Thus, the most recent, commercially available antibiotics need doctor's orders because the advantages thereof often are not much greater than the danger degree.

15 It is known that just because of the danger degree of some molecules it is highly desirable for the patient to get rid thereof in a very short time. Thus, physicians need to know ways and times of elimination of waste matter with absolute certainty.

20 Another disadvantage of the last-generation antibiotics relates to the action field thereof. The latter is extremely limited: what is active against gram-positive bacteria is not the same against gram-negative bacteria or mycetes.

25

Still another disadvantage is that such antibiotics, actually being synthesis molecules and then as such foreign and unknown to our biological system (real chemotherapeutic agents), are considered as foreign molecules so that the defence mechanisms react against them producing the phenomenon of the concurrent reactions (undesired effects in humans) and cause bacteria to be antibiotic-fast.

The present invention seeks to provide an antibiotic which unlike the present antibiotics is of quite natural origin and essentially non-toxic, does not produce concurrent reactions, has a broad spectrum and is active against both gram-positive and gram-negative bacteria as well as mycetes and Candida Albicans.

The inventor directed his investigations towards the superior vegetal world searching the solution of the above-mentioned problems by combining substances of certain natural origin, the efficacy of which has never changed.

The proposed aim is not to resort in any way to manipulations or alterations but only to the mere, simple admixture of natural products or fractions thereof on the base of the following reflections:

a) really natural substances are extremely active and, if this is not the case, it is all the fault of the human inexperience which is not able to duly use what available in nature;

b) natural substances do not lose efficacy in time: it

should be appreciated, for example, that pyrethrum is still an irreplaceable insecticide unlike D.D.T. (dichlorodiphenyltrichloroethane) which was very active when discovered but is now obsolete and inactive due to the acquired immunity of insects;

c) although "vegetal" has been hitherto synonym of light, delicate, perhaps not very effective, the plants are full of antibiotics from roots to leaves which need only to be found out;

d) natural antibiotics, however, have a specific task in the organization of the plant to which they belong: if we look at something different, i.e. something which fulfils our purpose, we have to resort to suitable, specific compositions.

Under these circumstances a number of tests for measuring the antibacterial activity of many plants as well as the extracts and the volatile fractions thereof have been carried out. The antibacterial action has not only been considered as a simple activity directed to struggle against bacteria but a rather complex, well-balanced activity resulting from multiform synergism aiming at changing microclimate, metabolic exchanges, permeability of the cell walls, and diffusibility of the active principle. In view of this the volatile fractions have nearly always proved to be most active.

Thus it is provided a composition of volatile active fractions which is capable of performing complex, co-ordinated, well-balanced actions and is formed of two essential oils, i.e. Tea Tree Oil or Essential Oil of

Malaleuca Alternifolia and Essential Oil of Thyme in which a synergism has been surprisingly detected in a determined range:

Tea Tree Oil	from 50% to 90% by weight
White Thyme or	
Wild Thyme Essential Oil	from 50% to 10% by weight

The characteristics of the two oils are widely cited in the literature. The essential oil of thyme is known as a mild antiseptic because of the substantial presence of phenols such as thymol which finds medical applications as vermicide and enteral antiseptic and disinfectant as well as antiseptic and disinfectant of sores, wounds and skin disease. The activity of Tea Tree Oil towards mycosis is likewise known.

However, the activity of the specific mixture has been proved to be clearly higher than the sum of the single components. Also the broad spectrum shows that the performed actions are very much and very complex: of course, a contribution is given by the fact that the described antibiotic includes not only components having specific antibacterial activity but also other components of the essential fraction which act synergically and in extremely positive manner even if the action mechanisms are not exactly known.

A first advantage of the natural antibiotic according to the invention is that because of its volatility it does not feel the effects of the barriers (epithelia) that the body raises for its defence, this being to its action rate advantage.

Another advantage is that it is an apolar, non-ionized composition and then hardly inactivated by the organic matter.

5 A further advantage is that said antibiotic is active for a long time and its action rate is very high.

Another advantage is that said antibiotic may be applied both externally and internally, and the metabolic ways of elimination are the usual ways for the food as such antibiotic is a foodstuff which is
10 non-toxic in the recommended doses and can be easily eliminated.

A further advantage is that the antibiotic does not give accumulation phenomenons.

15 Still another advantage is that it has the minimum toxicity and then can be prescribed by the doctor with more confidence in all of the cases in which the affection is not acclaimed. For example, a dentist does not resort to antibiotics except in case of absolute necessity and does not prescribe them on the
20 first swelling or the first abscess signs. However, the latency period brings to an acclaimed infection because of the lack of treatment.

The antibiotic of the present invention can be used immediately to struggle against bacteria because it is
25 effective without being toxic and does not cause any other trouble such as the antibiotic-fastness.

The advantages for the patient are enormous because the prevention of an infection entails the elimination of many after-effects such as pain, swelling, etc.

30 Another advantage is that no medical prescription is

needed for buying such antibiotic and then its diffusion is not limited.

The natural composition of the present invention, as illustrated thereafter by microbiological tests and photos, has a broad spectrum including also mycetes, which are even more diffused forms very hard to fight by the usual antibiotics.

Following the carried out experiments the antibiotic has proved to be active both for internal and external use and can be exhibited under a variety of pharmaceutical preparations: capsule, tablet, powder, cream, ointment, lotion, paste, solution, syrup.

The tested product having the best effectiveness/concentration ratio has the following composition:

Tea Tree Oil	70% by weight
Thyme Essential Oil	30% by weight

In some cases it is possible to add to such a composition the Eucalyptus essential oil which has proved to have high antibiotic characteristics.

The concentration of Eucalyptus essential oil ranges from 10% to 50% by weight.

The use of such substance, however, is limited to antibiotic compositions only for adults as it can cause the children's glottis spasm.

MICROBIOLOGICAL TESTS

In order to demonstrate that the activity of the antibiotic according to the present invention is higher than the sum of the activities of the single

components, the technique normally used for the antibiograms is applied. Even if the antibacterial activity of the single components is known, it could not be foreseen that such specific mixture was so effective as to be one of the most effective antibiotics available.

The annexed photos indicated at 1 to 3 show the inhibition halos of the two separate components (A= Tea Tree Oil; B= Thyme E.O.) and the admixture (C) thereof with respect to different cultures of gram-positive and gram-negative bacteria and Candida.

It can be seen from the same photos that the spectrum of the antibiotic according to the invention is very broad and is particularly effective against Candida besides excellently struggling against gram-negative and gram-positive bacteria.

During the first tests, the natural antibiotic was left alone in order not to alter data of the other antibiotics. The tested antibiotic is a mixture of 2 essential oils, i.e. Tea Tree Oil and Thyme Essential Oil in the amount of 70% and 30%, respectively.

Such mixture was put in contact with different cultures of gram-positive and gram-negative bacteria and Candida Albicans; the same cultures have been tested with the single natural substances in order to prove the synergical effect of the mixture.

Description of the tests:

10 mg of the antibiotics Tea Tree Oil and Thyme Essential Oil were deposited on sterile disks and then

deposited on:

1) TSA (Tryptic Soy Agar) containing 1 ml of germ broth with Staphylococcus Aureus for the test with gram-positive bacteria;

5 2) TSA (Tryptic Soy Agar) containing 1 ml of germ broth with Escherichia Coli for the test with gram-negative bacteria;

3) Sabouraud's agar containing 1 ml of germ broth with Candida Albicans for the test with mycetes;

10 The same bacterial strains were subjected to antibiogram to compare the inhibition halos obtained after 24 h incubation. The inhibition halos gave the following values:

15 1) Staphylococcus Aureus (photo 1):

Tea Tree Oil = 10 mm	Erythromycin E 15 mg = 20 mm
Thyme E.O. = 18 mm	Gentamicin GN 10 mg = 18 mm
New Antibiotic	= 26 mm
Cephalothin KF 30 mg	= 20 mm
20 Cephuroxin CXM 30 mg	= 25 mm
Clindamycin 2 mg	= 20 mm
Co-Trimoxazol sat 25 mg	= 18 mm
Oxacillin OX 1 mg	= 16 mm
Penicillin P 10 I.U.	= 0 (fast)

25

2) Escherichia Coli (photo 2)

Tea Tree Oil = 10 mm	Amikacin AK 30 mg = 14 mm
Thyme E.O. = 23 mm	Aztreonah ATH 30 mg = 24 mm
New Antibiotic	= 27 mm
30 Carbenicillin CAR 100 mg	= 21 mm

	Cefotaxin CTX 30 mg	= 25 mm
	Chloramphenicol C 30 mg	= 18 mm
	Fosfomycin FOS 50 mg	= 14 mm
	Mezlocillin MEZ 75 mg	= 18 mm
5	Rifampin RP 30 mg	= 15 mm

Note: antibiotics used for antibiogram are specific for enterobacteria.

10 3) Candida Albicans (photo 3)

Tea Tree Oil = 8 mm

Thyme E.O. = 23 mm

New Antibiotic = 30 mm

15 Conclusions:

1) As can be seen from the inhibition halos the antibiotic of the present invention, formed of the combination of Tea Tree Oil and Thyme Essential Oil, has an optimum synergism with respect to the single
20 Tea Tree Oil and Thyme Essential Oil.

2) The inhibition halo of the new antibiotic is also broader than the inhibition halos of the antibiograms of the single components.

25

3) The new antibiotic shows a very effective action also against Candida which is, as known, antibiotic-fast, some antibiotics even assisting the growth of the latter.

30

It is self-evident from the foregoing that the antibiotic of the present invention can be used alone in a number of compositions for therapeutic use under the form of capsule, tablet, powder, cream, ointment, lotion, paste, solution, syrup, etc.. A variety of ingredients well known in the art may be used in such compositions to achieve the desired characteristics. Therefore, it should be understood that the present invention can be accomplished in a different manner from that specifically described without departing from the scope of the annexed claims.

Claims

1. A natural broad-spectrum antibiotic characterized in that it is formed of a mixture of Tea Tree Oil (Essential Oil of *Malaleuca Alternifolia*) and Thyme Essential Oil in the ratio of 50-90% and 50-10% by weight, respectively.

2. A natural broad-spectrum antibiotic characterized in that it is formed of a mixture of Tea Tree Oil (Essential Oil of *Malaleuca Alternifolia*) and Thyme Essential Oil in the ratio of 70% and 30% by weight, respectively.

3. Use of a mixture of Tea Tree Oil and Thyme Essential Oil in the ratio of 50-90% and 50-10% by weight, respectively, as antibacterial active principle in pharmaceutical and food compositions.

4. Mixtures of essential oils (volatile fractions) of vegetal origin and antibacterial activity consisting of Tea Tree Oil and Thyme Essential Oil in the ratio of 50-90% and 50-10% by weight, respectively.

4. The mixtures of essential oils (volatile fractions) of vegetal origin and antibacterial activity of the preceding claim, characterized in that such mixtures further include Eucalyptus essential oil in the amount of 10-50% by weight.

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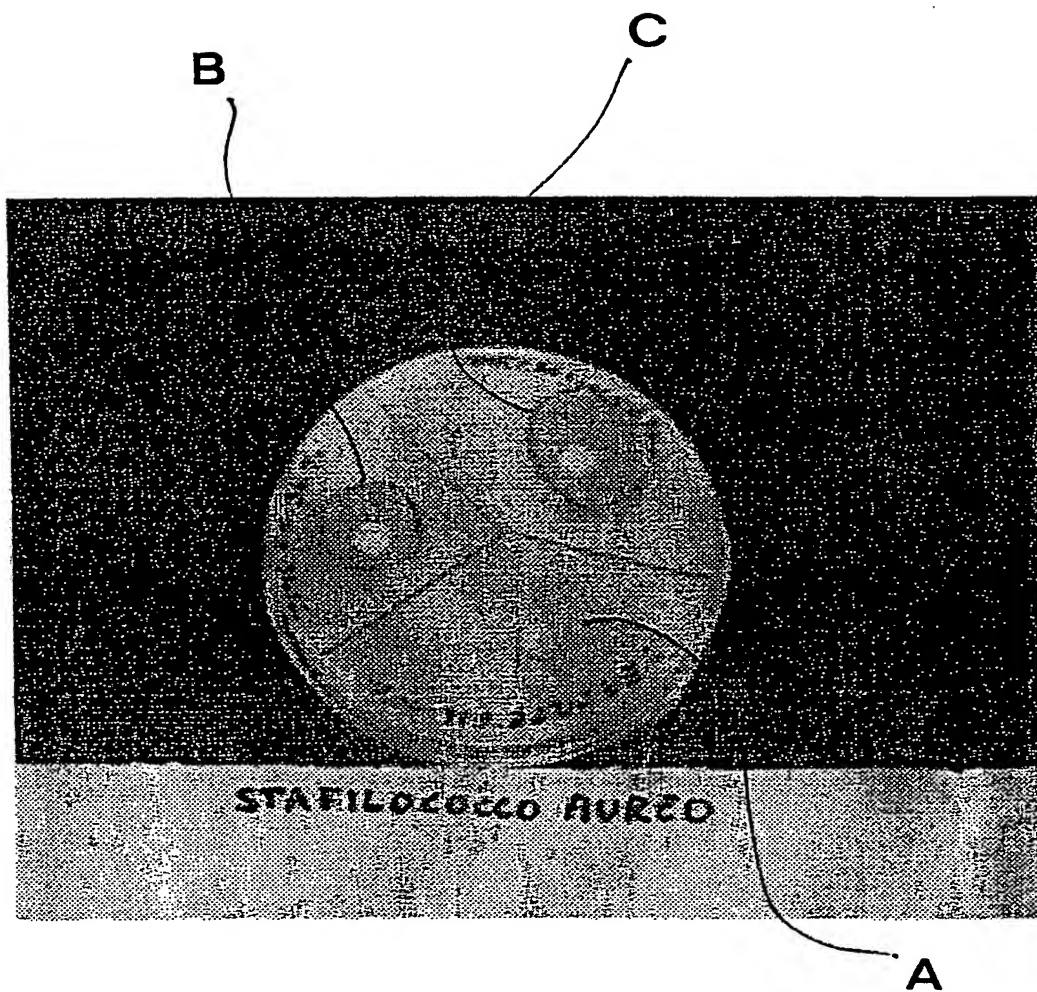
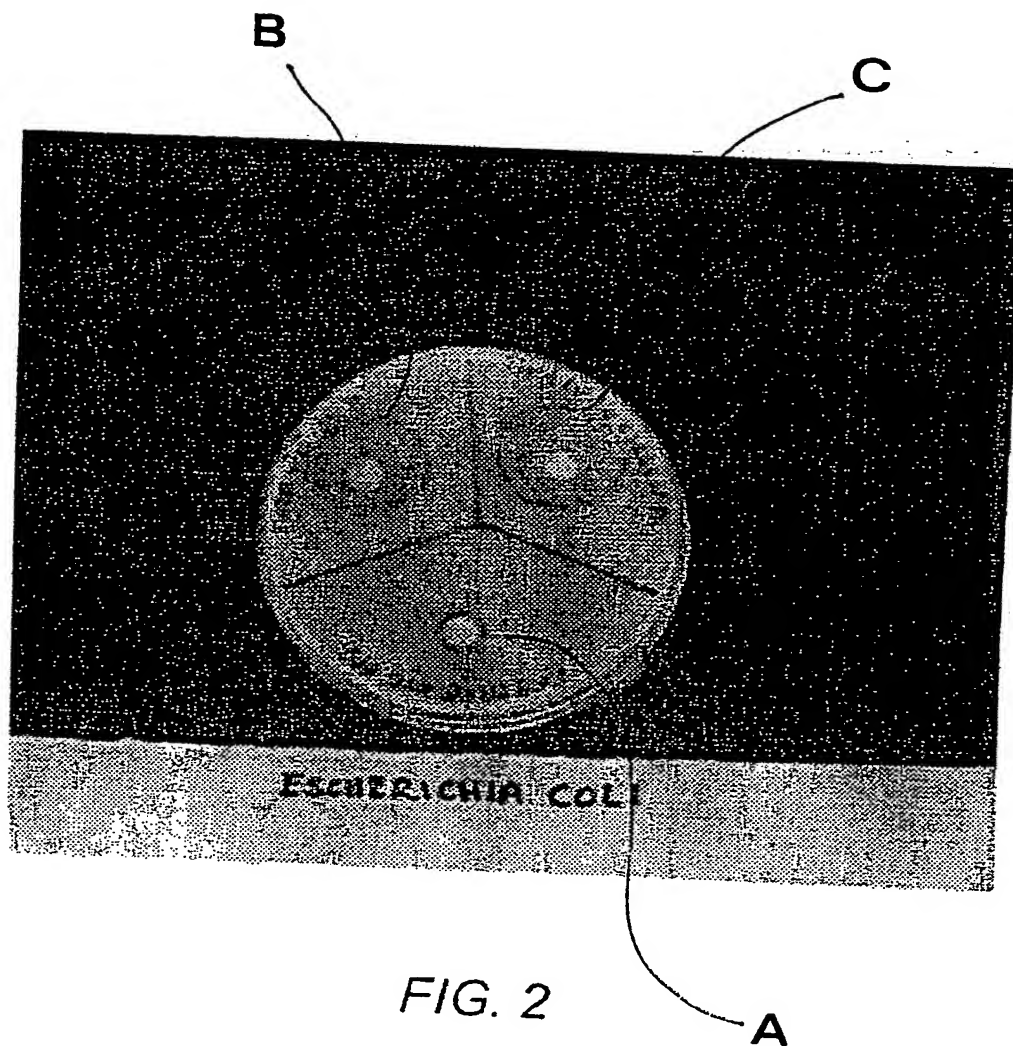


FIG. 1

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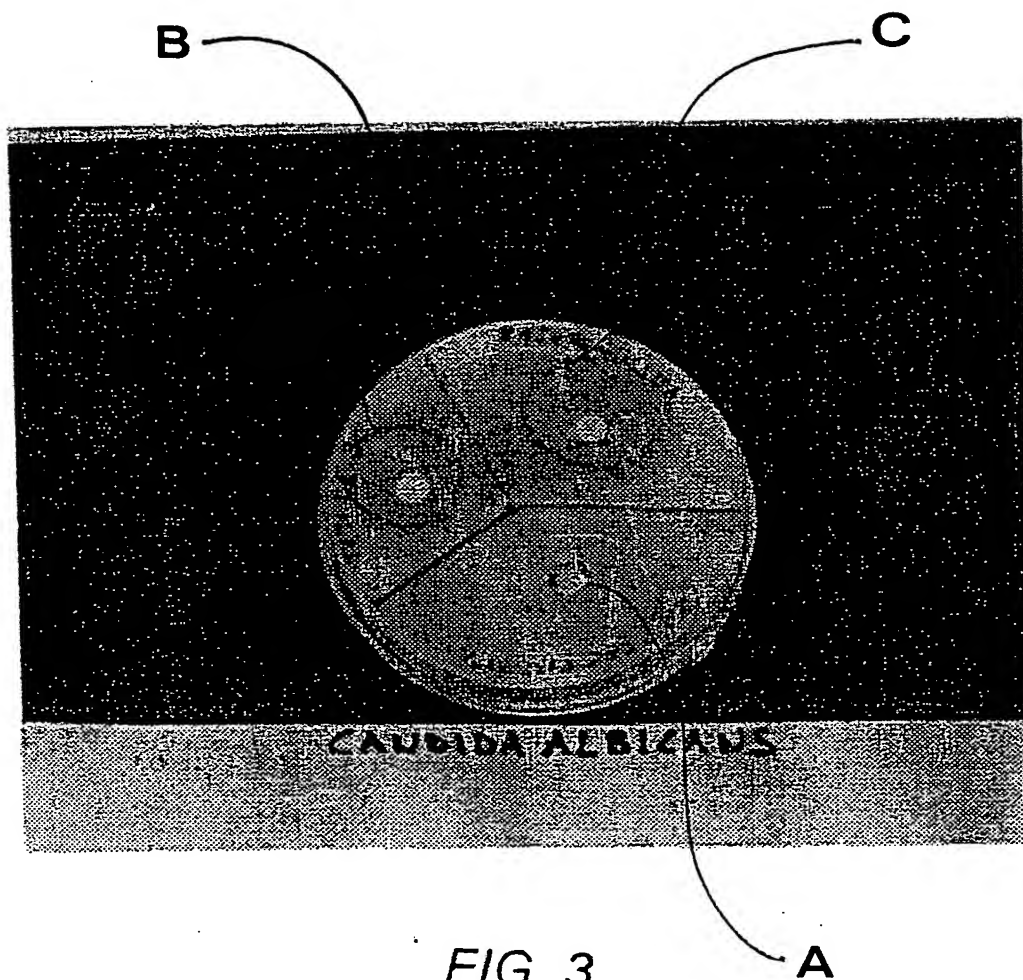


FIG. 3

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INTERNATIONAL SEARCH REPORT

Int. Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K35/78

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

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C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FR 2 706 770 A (PELLETIER JACQUES) 30 December 1994 see the whole document	1-5
X	RAMANOELINA A.R.P. ET AL.: "CONTRIBUTION A L'ETUDE DE L'ACTION ANTIBACTERIENNE DE QUELQUES HUILES ESSENTIELLES EXTRAITES DE PLANTES MALGACHES." ARCHIVES DE L'INSTITUT PASTEUR DE MADAGASCAR, vol. 53, no. 1, 1987, pages 217-226, XP002055775 see the whole document	1-4

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Date of the actual completion of the international search

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Int. Application No

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Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	A.M. JANSSEN ET AL.: "SCREENING OF SOME ESSENTIAL OILS FOR THEIR ACTIVITIES ON DERMATOPHYTES" PHARMACEUTISCH WEEKBLAD SCIENTIFIC EDITION, vol. 10, 1988, pages 277-280, XP002055776 see the whole document	1-5
X	--- S.M. HUSSEIN AYOUB: "ANTIBACTERIAL AND ANTIFUNGAL ACTIVITIES OF SOME LIBYAN AROMATIC PLANTS." PLANTA MEDICA, vol. 56, no. 6, December 1990, pages 644-645, XP002055777 see the whole document	1-5
X	--- MARIA LIS-BALCHIN ET AL.: "BIOACTIVITY OF NEW ZEALAND MEDICINAL PLANT ESSENTIAL OILS." ACTA HORTICULTURAE, no. 426, 1996, pages 13-30, XP002055778 see the whole document	1-5
A	--- PATENT ABSTRACTS OF JAPAN vol. 096, no. 007, 31 July 1996 & JP 08 059453 A (KANEBO LTD), 5 March 1996, see abstract	1-4

INTERNATIONAL SEARCH REPORT

Information on patent family members

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